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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,648	07/23/2003	Peter B. Heifetz	2075USCON8	9729

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EXAMINER	
LUNDGREN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1639	

MAIL DATE	DELIVERY MODE
02/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/625,648	HEIFETZ ET AL.	
	Examiner	Art Unit	
	Jeff Lundgren	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29,34-36 and 41-59* is/are pending in the application.

4a) Of the above claim(s) *42,44-51 and 53-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28, 29, 34-36, 43 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Supplemental Action

This Action is issued in response to an error made by the Office, wherein an Action was inadvertently mailed out as a Non-final Action (January 23, 2008). Accordingly, this Office Action is now being mailed, and is mailed out as a Final Action.

Election/Restrictions

Applicant's election without traverse of SEQ ID NO: 12, wherein alanine at position 226 is replaced by threonine, in the reply filed on October 22, 2007, is acknowledged.

Claims 28, 29, 34-36 and 41-59, are pending in the instant application; claims 42, 44-51 and 53-59 are withdrawn as being directed to a non-elected invention; claims 28, 29, 34-36, 43 and 52, are the subject of the Office Action below.

Previous Grounds of Rejection - Withdrawn

All outstanding rejections in the Office Action mailed on September 14, 2006, are withdrawn in view of Applicants' amendments to the claims.

New Grounds of Rejection – Necessitated by Amendment

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28, 29, 34-36, 43 and 52, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28 and 35 are indefinite for reciting "at a position corresponding to" because it is not clear to what breadth that any given substitution in SEQ ID NO:12 would be for any other protein considered to be a protox enzyme.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28, 29, 34-36, 43 and 52, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for transforming the plastome of a tobacco plant with the specifically claimed mutations at position 226 of SEQ ID NO:12, does not reasonably provide enablement for any plant. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors include, but are not limited to:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The standard for determining whether the specification meets the enablement test was first stated in *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), and asks if the experimentation needed to practice the invention undue or unreasonable.

The claimed invention is enabled if any person skilled in the art can make and use the invention without undue experimentation. The focus is on 'undue' rather than on 'experimentation' (*In re Wands*, at 737, 8 USPQ2d at 1404; see also *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988)).

A patent need not teach what is well known in the art (In re Buchner, 929 F.2d 660, at 661, 18 USPQ2d 1331, at 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, at 231 USPQ 81, at 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, at 1463, 221 USPQ 481, at 489 (Fed. Cir. 1984)).

Determining whether claims are sufficiently enabled by the specification is based on underlying findings of fact. *In re Vaeck*, 947 F.2d 488, at 495, 20 USPQ2d 1438, at 1444 (Fed. Cir. 1991); *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, at 576, 224 USPQ 409, at 413 (Fed. Cir. 1984).

The Breadth of the Claims

The claims are overly broad because the claims encompass the genetic transformation of the plastids of all plants, wherein a chimeric gene comprising SEQ ID NO:12 having a 226 mutation of Ala → Thr, and a promoter capable of expressing the DNA molecule in a plastid to produce a mature enzyme in the plastid.

The Nature of the Invention, and the Level of One of Ordinary Skill

As it is with many inventions in the biotechnology arts, the art related to plant genetics and the genetic transformation of plants is multidisciplinary. Applicants' claimed invention relates to a number of core technologies and scientific concepts including the selection of certain vectors, the required expression elements within the vector, and the chemistry and microbiology of gene delivery.

Those of skill in the art have a strong understanding of the inter-relationship between each of the core concepts, and understand where the specification lacks guidance that certain solutions are provided for in the art as routine.

The Amount of Guidance, and the Existence of Working Examples

In the *Background of the Invention*, Applicants summarize the importance of understanding biosynthetic pathways that lead to the production of chlorophyll and heme, the physiological importance of these proteins to plants, and the role that protox plays in the

synthesis of these proteins (pages 1 and 2). Applicants also explain how it would be advantageous to develop a plant with a protox enzyme that is resistant to given herbicides through site directed mutagenesis, and expressing such an enzyme in the plastid (pages 2-6).

In the *Summary of the Invention* (pages 6-9), Applicants generally describe that the invention is directed towards genetically modified plants, wherein the plants have improved protox activity with reduced toxicity to herbicides, wherein the genetic modification is done at the plastome level. Applicants state that plants that would be useful for practice of the invention include barley, wheat, sorghum, rye, oats, turf and forest grasses, as well as sugar cane, cotton, soybean and tobacco (page 7, first paragraph).

In addition to providing certain definitions related to the invention (pages 11-15), the *Detailed Description of the Invention*, expands upon Applicants summary of the invention. This expanded description provides certain routine description of procedures related to plant genetics, and how such procedures should relate to the disclosed invention (pages 15-73).

Applicants provide a number or working examples, some of which are related to the claimed invention.

Examples 1-8 are directed to the isolation of various plant protox genes, such as wheat, soybean, cotton and others (pages 74-80). Examples 9-12 relate to protox clone testing regarding herbicides (pages 81-85). Examples 13-15 relate to certain protox mutants, and Example 16 relates to the mutant of SEQ ID NO:12 with the Ala → Thr mutation at position 226. Examples 17-19 are related to other mutant protox enzymes.

Examples 20-47 relate to certain gene-based transformation components of the invention, including certain vectors and components such as promoters, but do not exemplify a working example of a plant having a genetically modified plastome that expresses a mutant protox in a plastid other than a tobacco plant.

The State of the Prior Art and the Level of Predictability in the Art

At the time that the invention was filed (the priority date for claim 28 is February 28, 1997), there existed a number of challenges for genetically modifying the plastome in plants other than the tobacco plant. For example, Lutz (Lutz *et al.*, Plant Physiology 145:1201-1210,

2007) teaches that transformation of a plant on the plastome level was only routine for tobacco plants:

> "For example, a typical Arabidopsis leaf cell contains approximately 120 chloroplasts and a total of 1,000 to 1,700 ptDNA copies (Zoschke et al., 2007) while an average tobacco (Nicotiana tabacum) leaf cell carries approximately 100 chloroplasts and approximately 10,000 ptDNA copies (Shaver et al., 2006). Transformation of the nuclear genome is routine in higher plants and is reviewed in this Focus Issue of Plant Physiology. Plastid ***transformation is routine only in tobacco*** (Svab et al., 1990; Svab and Maliga, 1993), but has rapidly expanded to diverse crops including potato (Solanum tuberosum; Sidorov et al., ***1999***), tomato (Solanum lycopersicum; Ruf et al., ***2001***), lettuce (Lactuca sativa; Lelivelt et al., ***2005***; Kanamoto et al., ***2006***), soybean (Glycine max; Dufourmantel et al., ***2004***), cotton (Gossypium hirsutum; Kumar et al., ***2004***), cauliflower (Brassica oleracea; Nugent et al., ***2006***), and poplar (Populus alba; Okumura et al., ***2006***). Transformation of mitochondrial DNA remains a challenge for the future."

Lutz, page 1201, first paragraph in col. 2 (emphasis added).

Certain specific aspects as to why gentically modifying the plastome requires undue experimentation are explained by Kanevski (Kanevski *et al.*, Plant Physiology, January 1999, Vol. 119, pp. 133–141). Kanevski teaches the transformation of a sunflower plant at the plastome level based on an understanding of the tobacco plant, but shows how technical obstacles arise to a successful transformation, and include factors such as incompatibility at the level of translation, or protein folding:

> "This is followed by transformation of the plant system to express the chimeric genes and produce protein. The full gene from Synechococcus PCC6301 was transcribed into mRNA, but the mRNA was not translated into protein. ***At this stage, it is unknown whether there is incompatibility at the level of translation, or if the protein, once produced, is unable to assemble correctly using the indigenous folding machinery.*** Western analysis indicated that if protein is produced it is transient and does not accumulate enough to be detected by antibodies raised against the cyanobacterial large subunit. However, in those cases in which higher plant/cyanobacterial rbcL chimeras are of interest (Gutteridge et al., 1989a) and have proved intractable using E. coli expression and refolding, this system might provide an alternative approach, one that can supply the amounts of enzyme required for detailed structural analysis using crystallography."

Kanevski, page 139, first paragraph in col. 1 (emphasis added).

The Quantity of Experimentation

Based on the art cited above, the unresolved issues in the relevant art pertaining to the genetic transformation of a non-tobacco plastome, the amount of non-routine experimentation required would be high. Accordingly, in order to enable the invention as claimed, one of ordinary skill in the art would have to resort to undue experimentation.

Conclusions

No claim is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should

Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Schultz, can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL

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